# DSDISP

# Version 3.0

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# 1 Model

#### Abstract

In recent years, infectious diseases such as AIDS have greatly grown in prominence. Also, with the emergence of new diseases like SARS, the sporadic outbursts of ebola, plague and Creutzfeldt-Jakob disease (CJD) and the continuing bioterrorist threat of small pox, we require a better understanding of the spread of infectious diseases. A common way to study epidemics is to divide the population into three main groups — Susceptible, Infected, and Recovered (known as the SIR model). The entire population can also be differentiated according to demographic characteristics and the infected group can then be subdivided according to the stage of infection. Here we present a combined model that contains such a demographically differentiated population and allows each demographic group to pass through multiple stages of infection. This model is general enough to allow for the simulation of different diseases through populations divided according to various demographic categories, such as age, behavioural risk or income level. We have written a program in MATLAB to simulate this model and this program is available for use.

# 1.1 Theoretical Development

# 1.1.1 Introduction

To effectively study the spread of infectious diseases, we divide the population into three main stages — susceptible (S), infected, (I) and recovered (R). We then divide these stages into various demographic groups. This allows us to take into account different attributes of people such as general susceptibility, infectivity, number of contacts, rate of disease progression, death rate and so on. The possible demographic categories include age, income level, occupation, number of contacts, etc. We then further subdivide the infected groups into various infection stages. This allows us to take into account varying infectivity and death rates at different stages of the diseases. Although not yet included in

the model, it would also be possible to model behaviour changes with different infection stages.

People enter the demographically differentiated susceptible groups at different rates through birth and migration. As they get infected, at a rate dependent on that demographic group, they enter the first infection stage. Then, depending on the rates of disease progression, they proceed through the remaining infection stages, before entering the recovered population. From any stage, they leave the model population at a rate derived from natural death and migration.

This is a good model for viral diseases that confer permanent immunity after a person has recovered. It is also possible to expand this model, with user-defined modules, to include diseases with temporary immunity.

#### 1.1.2 **Model Definition**

DSDISP stands for Differential Susceptibility Differential Infectivity Staged-Progression. As described in the introduction, we are demographically dividing the population into different groups that progress through various infection stages. For this model, we will consider n demographic groups and m infection stages. See Figure 1 for the basic layout of the model. See (1) for the dynamics of the model and Table 1 for a description of the parameters used in this model. All parameters except  $\lambda$  are constant in time. We will define  $\lambda$  in §1.1.3.

In the current version of the model, people cannot move between demographic groups. Once someone enters a certain susceptible group in Figure 1, (s) he may only move horizontally through the infection stages of that demographic group. The groups in this model may therefore not be used to represent locations when the model includes migration between the locations. The groups can be used to represent locations only if people always return to their home location. Also, if the groups are used to represent age, the lifespan of the disease must be significantly shorter than the size of the age groups.

Eventually, we would like to add the ability to move between demographic categories. We would also like to include multiple strains of disease in a future version of the model.

$$\frac{dS_i(t)}{dt} = \Lambda_i - (\mu_{iS} + \lambda_i(t))S_i(t)$$
(1a)

$$\frac{dS_i(t)}{dt} = \Lambda_i - (\mu_{iS} + \lambda_i(t))S_i(t) \tag{1a}$$

$$\frac{dI_{i1}(t)}{dt} = \lambda_i(t)S_i(t) - (\gamma_{i1} + \mu_{i1})I_{i1}(t) \tag{1b}$$

$$\frac{dI_{ij}(t)}{dt} = \gamma_{i,j-1}I_{i,j-1}(t) - (\gamma_{ij} + \mu_{ij})I_{ij}(t) \qquad \text{for } 2 \le j \le m \tag{1c}$$

$$\frac{dR_i(t)}{dt} = \gamma_{im}I_{im}(t) - \mu_{iR}R_i(t) \tag{1d}$$

$$\frac{dI_{ij}(t)}{dt} = \gamma_{i,j-1}I_{i,j-1}(t) - (\gamma_{ij} + \mu_{ij})I_{ij}(t) \quad \text{for } 2 \le j \le m \quad (1c)$$

$$\frac{dR_i(t)}{dt} = \gamma_{im}I_{im}(t) - \mu_{iR}R_i(t)$$
(1d)

for  $1 \le i \le n$ .

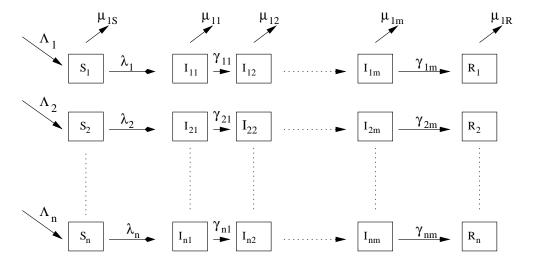


Figure 1: Schematic for the DSDISP model with n demographic groups and m infection stages. People enter different susceptible groups through birth or migration at different rates dependent on the demographic characteristics of that group. They get infected at a rate,  $\lambda$ , and then progress through various infection stages at rates of disease progression,  $\gamma$ , before entering the recovered state. They leave the population at a rate,  $\mu$ , through death and migration.

# 1.1.3 Definition of the rate of infection $(\lambda)$

The core of (1) lies in the definition of  $\lambda_i$ . We define  $\lambda_i$  as the rate at which the susceptible population in demographic group i gets infected and progresses to stage  $I_{i1}$ . We calculate this as the sum of the rate of disease transmission from each infected subgroup,  $I_{kj}$  for  $1 \le k \le n$  and  $1 \le j \le m$ , to the susceptible group,  $S_i$ , in (2). This means that a susceptible person in group i can get infected by an infected person in any group or infection stage.

$$\lambda_i(t) = \sum_{k=1}^n \sum_{i=1}^m \lambda_{ikj}(t) \tag{2}$$

Here,  $\lambda_{ikj}$  is the rate of disease transmission from the infected people in subgroup  $I_{kj}$  to the susceptibles in  $S_i$ . We calculate this in (3) as a product of the number of contacts, per unit time, that each individual in group i has with demographic group k; the probability of transmission per contact between someone in group  $I_{kj}$  and group  $S_i$ ; and the probability that out of all people in demographic group k, the contact is in infection stage j. See Table 2 for a summary of the parameters used in this definition.

 $S_i(t)$ : The number of susceptibles in demographic group i. Units: People.

 $I_{ij}(t)$ : The number of infecteds in demographic group i and infection stage j. Units: People.

 $R_i(t)$ : The number of recovereds in demographic group i. Units: People.

 $\lambda_i(t)$ : Rate at which susceptibles in demographic group i get infected. Units: Time<sup>-1</sup>.

 $\Lambda_i$ : The inward migration rate for demographic group i. Units: People/Time.

 $\gamma_{ij}$ : The rate of disease progression for a person in demographic group i and infection stage j. Units: Time<sup>-1</sup>.

 $\mu_{iS}$ : =  $\mu_{im} + \mu_{id}$ . The total loss of population from group  $S_i$ . Units: Time<sup>-1</sup>.

 $\mu_{ij}$ : =  $\delta_{ij} + \mu_{im} + \mu_{id}$ . The total loss of population from group  $I_{ij}$ . Units:

 $\mu_{iR}$ : =  $\mu_{im} + \mu_{id}$ . The total loss of population from group  $R_i$ . Units: Time<sup>-1</sup>.

 $\mu_{im}$ : The natural migration rate out of the population for demographic group i. Units: Time<sup>-1</sup>.

 $\mu_{id}$ : The natural death rate for demographic group i. Units: Time<sup>-1</sup>.

 $\delta_{ij}$ : The disease induced death rate for demographic group i in infectious stage j. Units: Time<sup>-1</sup>.

Table 1: Summary of the parameters in the DSDISP model. All parameters are nonnegative.

$$\lambda_{ikj} = \begin{pmatrix} \text{Number of} \\ \text{Contacts per} \\ \text{Unit Time} \end{pmatrix} \begin{pmatrix} \text{Probability of} \\ \text{Transmission} \\ \text{per Contact} \end{pmatrix} \begin{pmatrix} \text{Probability} \\ \text{Contact is} \\ \text{Infected} \end{pmatrix}$$

$$\lambda_{ikj}(t) = (r_{ik}(t)) (\alpha_i \beta_{kj}) \left( \frac{I_{kj}(t)}{N_k(t)} \right) \tag{3}$$

The term,  $(r_{ik})$ , gives the average number of contacts made by one person in demographic group i with all people in demographic group k, as defined in (5). We explain this term in more detail in §1.1.4. The transmissibility,  $(\alpha_i \beta_{kj})$ , is the probability that someone in  $I_{kj}$  infects a person in  $S_i$ , given that there is a contact between  $I_{kj}$  and  $S_i$ . It is the product of the susceptibility of group  $S_i$ ,  $\alpha_i$ , and the infectivity of subgroup  $I_{kj}$ ,  $\beta_{kj}$ . The term,  $(I_{kj}(t)/N_k(t))$ , gives the fraction of individuals in group k who are in infected stage  $I_{kj}$ . The denominator,  $N_k(t)$ , is the total population size in demographic group k as in (4). The product,  $r_{ik}I_{kj}/N_k$ , gives the average number of contacts between someone in demographic group i and the infected people in subgroup  $I_{kj}$ . Multiplying that by the probability of transmission gives the force of infection from subgroup  $I_{kj}$  to the susceptibles in demographic group i. Summing over all the infection stages gives the force of infection from all infecteds to the susceptibles in group i. Multiplying this quantity by the number of susceptibles as in (1) gives the rate of change of new infecteds in demographic group i.

$$N_k(t) = S_k(t) + \sum_{j=1}^{m} I_{kj}(t) + R_k(t)$$
(4)

$$r_{ik}(t) = c_i p_{ik} \frac{c_k N_k(t)}{\sum_{l=1}^n c_l N_l(t)} \qquad \text{with} \qquad p_{ik} = q_{ik} q_{ki}$$
 (5)

 $\lambda_{ikj}(t)$ : The rate of disease transmission from  $I_{kj}$  to  $S_i$ . Units: Time<sup>-1</sup>.

 $\alpha_i$ :  $\in [0,1]$ . The susceptibility of a person in  $S_i$ . Units: 1.

 $\beta_{ki}$ :  $\in [0,1]$ . The infectivity of a person in  $I_{ki}$ . Units: 1.

 $r_{ik}(t)$ : The average number of contacts each person in demographic group i has with group k per unit time. Units: Time<sup>-1</sup>.

 $c_i$ : The preferred number of contacts (per person per time) for people in demographic group i. Units: Time<sup>-1</sup>.

 $p_{ik}$ : The probability (or preference) for a contact between group i and group k. Units: 1.

 $q_{ik}$ : The desirability of a contact with group k for someone in group i. This can also be thought of as the acceptability, for contact, of group i for group k. Units: 1.

Table 2: Summary of parameters in the definition of  $\lambda$ . All parameters are nonnegative.

 $[\alpha_i] = 1$ 

## **Dimensional Analysis:**

Let [x] denote the units of x for some variable x.

$$[\beta_{kj}] = 1$$

$$[r_{ik}(t)] = \frac{\text{Contacts}}{\text{Time} \cdot \text{Person}} = \frac{1}{\text{Time}}$$

$$[p_{ik}] = 1$$

$$\left[\frac{I_{kj}(t)}{S_k(t) + \sum_{j=1}^m I_{kj}(t) + R_k(t)}\right] = 1$$

$$[\lambda_{ikj}(t)] = \frac{1}{\text{Time}}$$

Therefore,

### 1.1.4 Definition of the mixing

The pattern of contacts between different groups plays an essential role in determining the spread of disease, especially in sexually transmitted diseases. We assume people in each group behave the same way when selecting a partner, but have biases between groups. In other words, mixing within each group is assumed to be homogeneous but there is heterogeneous mixing among the groups.

This mixing between groups is one of the most important factors in modeling diseases. For sexually transmitted diseases, it depends on the desirability of an active individual, the acceptability of his/her potential contacts, and the availability of these potential contacts.

Let  $q_{ik}$  be the desirability of people in group i to have a contact from group k; that is,  $q_{ik}$  is the fraction of people in group k with whom an individual in group i desires forming a contact. Thus  $q_{ik}$  describes the desirability of people in group i to have a contact from group k. It is also the acceptability of people in group k to people in group i.

Under the condition that enough potential partners are available, the probability  $p_{ik}$  that a partnership forms between individuals from group i and group k, is the product of the availability of group i for group k,  $q_{ki}$ , and the desirability of group i for group k,  $q_{ik}$ , as in (5).

Note that we can also alternatively define  $p_{ik}$  as the preference for a contact between group i and group k. With this alternative definition, the  $p_{ik}$ 's are no longer restricted to being less than or equal to 1.

We define  $c_i$  to be the preferred number of social contacts per unit time for a person in group i. The probability that a contact is with a person from group k is  $c_k N_k / (\sum_l c_l N_l)$  where  $N_k$  is the total population size of group k defined in (4). This also characterizes the availability of contacts with partners in group k. Hence, the probability of a partnership forming between individuals from group i and group k is  $p_{ik}c_k N_k / (\sum_l c_l N_l)$  (Again, if we think of  $p_{ik}$  as a preference then this now becomes a preference of forming partnerships.)

The desirability matrix need not be symmetric (i.e.  $q_{ik} \neq q_{ki}$ , when  $i \neq k$ ), but the probability of a partnership forming is symmetric since  $p_{ik} = q_{ik}q_{ki}$  implies  $p_{ik} = p_{ki}$ . Also, we note that there is no constraint on  $\sum_{k} q_{ik}$ , which may be less than or greater than one.

Two special cases of the model (1) with the infection rate, (2) and (3), are the restricted mixing model when  $q_{ik}=0$  (hence  $p_{ik}=0,\ i\neq k$ ) and the proportional mixing model when  $q_{ik}=1$ , for  $\{i,k\}=1,\cdots,n$ .

We denote the number of contacts per unit time of people in group i with people in group k by  $T_{ik}$ . The number of contacts with people in group i that people in group i have is also  $T_{ik}$ , that is  $T_{ik} = T_{ki}$ . These are the balance constraints that need to be satisfied at all times. In multi-group models where an attempt is made to directly control the number of partnerships formed between groups, these balance conditions usually are artificially enforced. However, in the selective mixing model, the balance constraint

$$T_{ik} = p_{ik} \frac{c_k N_k}{\sum_{l} c_l N_l} c_i N_i = p_{ki} \frac{c_i N_i}{\sum_{l} c_l N_l} c_k N_k = T_{ki}$$
 (6)

is automatically satisfied. Thus, by using the acceptability  $q_{ik}$  or desirability  $q_{ki}$  of an individual from group i to an individual from group k as the primary control variable in these models (instead of the number of partners an individual from group i desires from group k), the balance constraints become a natural consequence of the model, rather than an artificially imposed constraint.

The number of contacts per individual per unit time in many multi-group models is assumed to be constant. When all  $q_{ik}$ 's equal one (proportional mixing), this is also true for the selective mixing model. However, if the mixing is biased, the actual number of contacts, denoted by  $r_i$ , for the selective mixing model will vary in time depending on the combination of desirability, acceptability, and availability.

Define P(i) as the probability that an individual in group i finds a partner from any group. The actual number of contacts per person in group i,

$$r_i = c_i P(i) = c_i \left( \sum_{k=1}^n p_{ik} \frac{c_k N_k}{\sum_l c_l N_l} \right), \tag{7}$$

reaches its maximum  $c_i$  only for the proportional mixing, where  $p_{ik} \equiv 1$  (i.e. everyone is acceptable as a partner). Remember that the average number of contacts per person (7) is the sum over the contacts with each demographic

If the mixing is biased, the acceptability and the availability of partners must be taken into consideration and a limitation may occur. Then  $p_{ik} \leq 1$ , and hence  $r_i \leq c_i$ .

However, we think of the  $p_{ik}$ 's as preferences, then it is possible for the actual number of contacts per person,  $r_i$ , to be greater than the preferred number of contacts,  $c_i$ .

#### 1.1.5Linear Analysis

The concept of a threshold condition is very important in epidemiology. The basic reproductive number,  $R_0$ , is the expected number of secondary infections from one infected person in a fully susceptible population during the duration of the entire infectious period. We are currently working on an analytic formulation for  $R_0$ .

However, we can evaluate the stability of the disease-free equilibrium through linear analysis. The disease-free equilibrium point of (1) is

$$S_i^* = \Lambda_i/\mu_{iS} \tag{8a}$$

$$S_i^* = \Lambda_i/\mu_{iS}$$
 (8a)  
 $I_{ij}^* = 0$  (8b)  
 $R_i^* = 0$ .

$$R_i^* = 0. (8c)$$

with  $N_i^* = S_i^* + \sum_{j=1}^m I_{ij}^* + R_i^*$ . There is a problem here if we have no inward or outward migration. We look at the four possible cases, for a given group, i, below.

- 1. If both  $\Lambda_i$  and  $\mu_{iS}$  are nonzero, we can use (8) above without any problems.
- 2. If both,  $\Lambda_i$  and  $\mu_{iS}$  are zero, the entire subspace,  $I_{ij}^* = 0$  with  $S_i^*$  and  $R_i^*$  arbitrary, is a continuum of fixed points. In this case, we define the disease-free equilibrium to be  $S_i^* = N_i(0)$ ;  $I_{ij}^* = 0$  (which is the only mathematical requirement for the fixed point); and  $R_i^* = 0$ . We perform

our linear analysis around the point where there is no recovered population in that group and the susceptible population is equal to the input initial total population of that group.

- 3. If  $\Lambda_i = 0$  and  $\mu_{iS} \neq 0$ , the disease-free equilibrium is  $S_i^* = 0$ ;  $I_{ij}^* = 0$ ; and  $R_i^* = 0$ .
- 4. If  $\Lambda_i \neq 0$  and  $\mu_{iS} = 0$ , we have no equilibrium point because we have inflow but no outflow. We do not perform any linear analysis.

It is possible in a multi-group model for a number of the cases above to simultaneously occur. If 4 is true for any of the groups, there is no disease-free equilibrium and we do not conduct any linear analysis. If 2 or 3 are true for any of the groups, we pick the coordinates of the disease-free equilibrium for those groups as described above; and continue with the rest as we would with  $1^1$ .

We calculate the Jacobian of the infecteds from our original system of equations (1). The first n equations correspond to the demographic groups in the first infection stage. The next n equations correspond to the demographic groups in the second infection stage and so on. The resulting Jacobian is  $(m*n) \times (m*n)$ . For our equations, the first n rows of the Jacobian are dense; while the remaining (m-1)\*n rows are sparse with entries in the main diagonal and the off-diagonal n rows across. The format of the Jacobian for a system with 2 demographic groups (n=2) and 3 infection stages (m=3) can be seen in (9). All other entries are 0.

As the actual entries of the Jacobian are too large to fit in one equation, we write them separately in (10)–(13). Let  $\bar{\imath}$  and  $\bar{k}$  correspond to the demographic group; and  $\bar{\jmath}$  correspond to the infection stage. We label the first n rows by  $\bar{\imath}$ . We label all columns for the first n rows by  $n*(\bar{\jmath}-1)+\bar{k}$ . (We remark here that  $\bar{\jmath}=1$  corresponds to the first n columns;  $\bar{\jmath}=2$  corresponds to the next n columns and so on.) Since we only have 2 nonzero diagonals in the remaining rows we can label them using only  $\bar{k}$  and  $\bar{\jmath}$ . The main diagonal elements are labelled by  $(n*(\bar{\jmath}-1)+\bar{k},n*(\bar{\jmath}-1)+\bar{k})$ . The off-diagonal elements are labelled by  $(n*(\bar{\jmath}-1)+\bar{k},n*(\bar{\jmath}-2)+\bar{k})$ .

The terms in the Jacobian are as follows:

• For the main diagonal in the first n rows  $(1 \le \bar{\imath} = \bar{k} \le n \text{ and } \bar{\jmath} = 1)$ :

<sup>&</sup>lt;sup>1</sup>The model breaks down if 3 is true for all the groups.

$$Df(\bar{\imath}, n*(\bar{\jmath}-1)+\bar{k}) =$$

$$\left(\frac{c_{\bar{i}}c_{\bar{k}}p_{\bar{i}\bar{k}}\alpha_{\bar{i}}\beta_{\bar{k}\bar{j}}}{\sum_{l=1}^{n}c_{l}N_{l}^{*}} - \sum_{k=1}^{n}\sum_{j=1}^{m}\frac{c_{\bar{i}}c_{\bar{k}}c_{k}p_{\bar{i}k}\alpha_{\bar{i}}\beta_{kj}I_{kj}^{*}}{\left(\sum_{l=1}^{n}c_{l}N_{l}^{*}\right)^{2}}\right)S_{\bar{i}}^{*} - \left(\gamma_{\bar{k}\bar{j}} + \mu_{\bar{k}\bar{j}}\right) \tag{10}$$

• For all other elements in the first n rows  $(1 \le \bar{\imath}, \bar{k} \le n, 1 \le \bar{\jmath} \le m$  and  $\bar{\imath} \ne n * (\bar{\jmath} - 1) + \bar{k})$ :  $Df(\bar{\imath}, n * (\bar{\jmath} - 1) + \bar{k}) =$ 

$$\left(\frac{c_{\bar{i}}c_{\bar{k}}p_{\bar{i}\bar{k}}\alpha_{\bar{i}}\beta_{\bar{k}\bar{j}}}{\sum_{l=1}^{n}c_{l}N_{l}^{*}} - \sum_{k=1}^{n}\sum_{j=1}^{m}\frac{c_{\bar{i}}c_{\bar{k}}c_{k}p_{\bar{i}k}\alpha_{\bar{i}}\beta_{kj}I_{kj}^{*}}{\left(\sum_{l=1}^{n}c_{l}N_{l}^{*}\right)^{2}}\right)S_{\bar{i}}^{*}$$
(11)

• For the main diagonal in the remaining rows  $(1 \le \bar{k} \le n \text{ and } 2 \le \bar{j} \le m)$ :  $Df(n * (\bar{j} - 1) + \bar{k}, n * (\bar{j} - 1) + \bar{k}) =$ 

$$-\left(\gamma_{\bar{k}\bar{\jmath}} + \mu_{\bar{k}\bar{\jmath}}\right) \tag{12}$$

• For the off-diagonal in the remaining rows  $(1 \le \bar{k} \le n \text{ and } 2 \le \bar{j} \le m)$ :  $Df(n*(\bar{j}-1)+\bar{k}, n*(\bar{j}-2)+\bar{k}) =$ 

$$\gamma_{\bar{k},\bar{\imath}-1} \tag{13}$$

If all the eigenvalues of this Jacobian, evaluated at the disease-free equilibrium point, are in the negative half-plane, then we can conclude that the disease-free equilibrium is locally asymptotically stable as small changes in the infected population will exponentially decay to zero.

We are also currently looking into ways of characterising the basic reproductive number as a distribution over the different demographic groups.

#### 1.1.6 Initialization

An added complication in any model with infected subgroups is the dependence of the behavior and the timing of the transient solutions of the epidemic model on the initial distribution of the infected populations among the subgroups. Hyman et al. show in [2] that even when the total number of infected individuals is fixed, the timing of the epidemic can be shifted by large amounts of time by varying the distribution of the initial infected population. This important observation is often overlooked in simulation studies comparing multi-group models. We develop a robust, systematic procedure for determining the initial distribution of the infected population when  $R_0 > 1$ , based on the progression of a natural epidemic that sets the timing of different multi-group models and allows them to be quantitatively compared.

Let  $f_{kj} = I_{kj}(0)/I(0)$ . The total initial infected population,

$$I(0) = \sum_{k=1}^{n} \sum_{j=1}^{m} I_{kj}(0),$$

is fixed and the goal is to prescribe a robust procedure to define the fractions,  $f_{kj}$ , where  $\sum_{k=1}^{n} \sum_{j=1}^{m} f_{kj} = 1$ . For models of the spread of infectious agents such as HIV, which have been

For models of the spread of infectious agents such as HIV, which have been spreading into populations that were originally free of this disease and thus have an initial background level of zero infections, we propose a procedure for defining the  $f_{kj}$  when  $R_0 > 1$  based on the idea that in nature the epidemic would have spread into the population from only a few infected individuals. The epidemic then grows from this small seed until by the time a noticeable number of individuals are infected, a natural balance between the infected subgroups is reached (thus defining  $f_{kj}$ ). When  $R_0 > 1$ , then the numerical pre-initialization procedure (NPP) is a simple approach to approximating the natural balance in the population that exists when an epidemic started in the past. In this procedure we distribute the initial infected population based on what it would be if a very small initial infected population was introduced in the distant past and grew to infect a given percentage of the population.

For example, to use the NPP simulation to distribute a 1% initial infection rate, the pre-initialization simulation is started with a much smaller infected population, say 0.01% of the population infected, and the equations are integrated until 1% of its population has become infected. This occurs at some time  $t^P$  (which depends on the distribution over the infected subgroups of the 0.01% pre-initialization infected population). At time  $t^P$  we stop the simulation and use the evolved distribution of the infected population from the pre-initialization simulation to define the relative fraction of the initial infected population in each group for the main simulation. Thus  $f_{kj} = I_{kj}^P(t^P)/I^P(t^P)$ , where the superscript P denotes the solution and ending time of the pre-initialization simulation. In numerical experiments we observed that the resulting initial conditions are almost independent of the distribution used in the pre-initialization simulation.

# 1.2 References

# References

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# 2 Code Description

# 2.1 Availability

On the website http://www.math.arizona.edu/~nakul/dsdisp.html, there is a link to the DSDISP model. This link contains this documentation and the code.

You can download the code here — for Windows and for Linux. There is documentation in html and pdf form.

## 2.2 Conditions for Use

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  - AND REQUIRE permission from the authors.

The code is distributed "as is". The authors will not assume any legal responsibilities arising from problems with this package.

This code is maintained by the authors. We welcome any suggestions for improvements and will gingerly and promptly take care of any bugs. Suggestions for modifications will be given serious consideration.

# 2.3 Code Documentation

- dsdisp.html (this document).
- dsdisp.pdf (this document).
- Help files on MATLAB scripts and functions.

### 2.4 To Obtain DSDISP code

# 2.4.1 Linux/UNIX

Download dsmodel.tar.gz from http://www.math.arizona.edu/~nakul/dsdisp.html.

### 2.4.2 Windows

Download dsmodelfiles.zip from http://www.math.arizona.edu/~nakul/dsdisp.html.

# 2.5 Code Installation

# 2.5.1 Linux/UNIX

After you have downloaded dsmodel.tar.gz, in the directory where you would like to create the subdirectory dsmodel/., type the following:

- 1. gunzip dsmodel.tar.gz
- 2. tar xvf dsmodel.tar

That should create the directory dsmodel and all its subdirectories.

#### 2.5.2 Windows

After you have downloaded dsmodelfiles.zip, you may use Winzip to extract the files into a directory of your choice. The extraction will contain the subdirectory dsmodel.

# 2.6 System/software Requirements

- There are no system requirements.
- Platforms: any LINUX/UNIX flavor or Windows<sup>2</sup>. We believe it will also work on a Macintosh although we have not tested that.
- MATLAB (version 6.1.0.450 (R12.1)). Although we believe the code should work on some earlier versions of MATLAB<sup>3</sup>.

# 3 Code Operation

# 3.1 Code Structure

The directory dsmodel has five subdirectories:

- code
- input
- output
- docs
- aux.

 $<sup>^2\</sup>mathrm{We}$  have tested the code for Windows XP.

 $<sup>^3</sup>$ There may be problems on earlier versions of MATLAB for Windows because the code requires a distinction between lowercase letters and capital letters.

- 1. The directory code contains all the scripts and functions that make up this code. The main driver, dsdisp.m, and plotfig.m are scripts while the rest of the subroutines are functions. This directory has three subdirectories for three MATLAB classes. The structure of these classes is explained in §3.2. The subdirectories are:
  - @xtype
  - @tautype
  - @xtautype.
- 2. The input directory contains the input files:
  - sp.in
  - SIfile
  - XTfile
  - MMfile.

These files are described in  $\S 3.4$ . This directory also contains a number of subdirectories that contain examples of input files that may be used for sample runs. See  $\S 3.7$  for more information on how to use these for sample runs.

- 3. The output directory contains the files created by the code where the data is saved. See §3.6.2 for the details of these files.
- 4. The docs directory contains this manual in pdf and html format.
- 5. The aux directory contains auxiliary files such as Maple scripts used in creating this code.

# 3.2 Data Structure

The data structure is broken into 4 primary classes:

- Scalars
- Variables dependent on the demographic group (xtype classes).
- Variables dependent on the infection stage (tautype classes).
- Variables depending on both the demographic group and the infection stage (xtautype classes).

The xtype, tautype and xtautype variables have been created as MATLAB classes. To see the methods associated with each class, type in

> methods <classname>

For example,

> methods xtype

will display the methods associated with the xtype class. You can then type

# > help <classname>/<methodname>

for help on a particular method. For example,

### > help xtype/printx

will show the help file for printing the values of an **xtype** class. We explain the format of each class in some detail below.

1. The xtype classes store data or parameters that are dependent on the demographic group. Examples of these include the susceptibility of the susceptible population, the inward migration rate and the susceptible and recovered population. To enable these variables to represent either absolute numbers or densities we represent the data in midpoint and endpoint format. The values at the midpoint can be used to represent the actual numbers or they can be assumed to represent densities and extrapolated to give values for the endpoints. We will use x to represent the demographic divisions. If, for example, we wish to use age as our demographic category, the values of x would represent the divisions of the different age groups. The bounds of the age bins would serve as the endpoints and these can then be used to find the midpoints of the age bins. An example of dividing a population into 6 age bins is (0, 5], (5, 12], (12, 18], (18, 22], (22, 55], (55, 100]. The corresponding x endpoints then are 0, 5, 12, 18, 22, 55 and 100. The corresponding midpoints are 2.5, 8.5, 15, 20, 38.5 and 77.5. The current version of the code only accepts endpoints for x and interpolates these to find the midpoints. Even if the demographic category is non-numeric (eg. gender or occupation), the code will still require x endpoints. For 4 demographic groups, the endpoints could simply be 1, 2, 3, 4 and 5. Note that the number of x midpoints is equal to the number of demographic groups and the number of x endpoints is one greater than the number of groups.

The xtype classes store these endpoint and midpoint values for x and store corresponding values for the variable. The code currently only deals with actual numbers (not densities) so the values of the variable at the midpoints corresponds to the actual number of that variable for that demographic group. In the above example of age groups, if the value for the first midpoint (2.5) for the recovered population is 240, then we can interpret that as 240 people in the recovered class between the ages of 0 and 5. The code now only accepts input data for the variable at the midpoints. It then extrapolates this to find the values of the variable at the endpoints. In this version of the code, we do not use the data at the endpoints. (In future versions of the code, we may also accept data at the endpoints and may work with distribution densities too.)

2. The structure of the tautype classes is similar to that of the xtype classes, except the variables are now a function of the infection stage,  $\tau$ , instead of the demographic group, x. There are no significant differences between these two classes except that the number of midpoints now is equal to the number of infection stages; and the  $\tau$  endpoints represent the time

frames of the different stages of the disease. We do not currently have any variables that are only dependent on the infection stage but we use this class of variables to create **xtautype** classes.

3. The xtautype store data or parameters that are dependent on both the demographic group and the infection stage. Examples of these include the infectivity of the people in the different infected subgroups and the number of infected people in each of these subgroups. They are created by combining the xtype and tautype classes, using the relative values of the different demographic groups and the infection stages. The sum of the data for the variable for both of these is then normalized to 1 and the two are raked together to create an xtautype class. The data is then multiplied by the value of the integral (specified in the input files — see §3.4.1).

**Raking:** We write the xtype data as a normalized  $(n \times 1)$  vector and the tautype data as a normalized  $(1 \times m)$  vector. We then multiply the x data by the  $\tau$  data to create a  $(n \times m)$  matrix — the data for the xtautype variable. This matrix is then multiplied by the value of the integral.

#### 3.3 Initial Conditions

The initial conditions are read in through input files. Nonzero values can only be specified for the initial susceptible and infected populations. The initial recovered population is always set to 0.

The model is run through an initialization procedure as described in §1.1.6. The pre-initialization infected population is read through input files as defined in §3.4. The code is then run until some threshold value of infecteds,  $I^P$ , is reached, at some time,  $t^{P-4}$ .

The time is then reset to 0 and the code run again with initial conditions defined by the state of the system at time  $t^P$ . The threshold value can be either set as the actual number of infecteds or as a percentage of total *pre-initialization* population. See §3.4 for details on how to set this threshold value.

At the time the threshold value is reached, the populations of all groups,  $S_i$ ,  $I_{ij}$  and  $R_i$ , and the time are stored in Sop, Iop, Rop and tronep, respectively. Note that Sop, Iop and Rop are stored as classes. The time rate of change of the populations are stored in Stop, Itop and Rtop. These are also stored as classes. The time the time the threshold is reached,  $t^P$ , is also stored in an output file as described in §3.6.2.

There is also a maximum set for initialization time,  $t^M$ . If the code does not reach the threshold value for the the infected population by  $t^M$ , it uses values in the different groups at time  $t^M$  as the new initial conditions, resets the time and continues. The code does display a warning.

If the pre-initialization infected population specified in the input files is greater than the given threshold,  $I^P$ , the code displays a warning, and does not

<sup>&</sup>lt;sup>4</sup>The actual time when the infected population reaches the threshold value is calculated by interpolating the two closest values from the output of MATLAB's ode45 command.

follow the pre-initialization procedure. It simply uses the given pre-initialization values as the initial conditions.

# 3.4 Input Files

# 3.4.1 sp.in

The main input file is sp.in contained in the directory dsmodel/input/. The parameters in this file is  $order\ sensitive$ . Changing the order of the parameters will result in an error that may or may not be displayed on the screen. The data from this file is read using the command textread. All variables that are stated to functions of x must have as many elements as the number of demographic groups. Similarly, all variables stated to be functions of  $\tau$  must have as many elements as the number of infection stages<sup>5</sup>. The input parameters are:

FlagData: A flag for the format of SIfile. Can be either 'FullMP', 'FullEP', 'SparseMP' or 'SparseEP'. Class: String. See §3.4.3 for details.

SIfile: The name of the file where the initial population data is stored. This contains the susceptible and infected populations used for the pre-initialization procedure. The recovered population is automatically set to 0. Class: String. See §3.4.3 for a description of the format of this file. Note that if the file is in the directory dsmodel/input/., the name will need to contain '../input/.' because the code is run from the directory dsmodel/code/..

XTfile: The name of the file where the data for the x and  $\tau$  variables is stored. Class: String. See §3.4.2 for details of the format of this file.

MMflag: A flag that determines the format of MMfile. This can be either 'MixingMatrix', 'MixingMatrixPP' or 'QCData'. Class: String. See §3.4.4 for more details.

MMfile: The name of the file where the mixing matrix is stored. Class: String. See §3.4.4 for details of the format of this file

Initflag: This is a string that can either be 'Percent' or 'Number'.

This is used to determine the threshold value for the total infected population size at which the code re-initializes. If 'Percent' is selected, then Initpc is used; if 'Number' is selected, then Init\_pop is used. Class: String.

Init\_pop:  $I^P$ . The number of infected people at which to re-initialize time when Initflag is set to 'Number'. Class: Scalar. Units: People.

<sup>&</sup>lt;sup>5</sup>It may be easiest to follow the format specified in the sample input files for sp.in as described in §3.7

Initpc: When Initflag is set to 'Percent', the number of infected people at which time is re-initialized is this percent of the **pre-initialization** population (the total population specified in SIfile). Class: Scalar. Units: Percentage.

inittime:  $t^M$ . The maximum time to run until re-initialization. If the infected population does not reach the threshold by this time, the code displays a warning and continues. This value needs to be a multiple of dtsave. Class: Scalar. Units: Time.

tfinal: The final time (after re-initialization) to integrate the system to. This value needs to be a multiple of dtsave. Class: Scalar. Units: Time.

dtsave: The time interval at which data is saved. This value needs to be a factor of tfinal and inittime. If it is not a factor of either one of the two, the code will run, but will display a warning. A large value of dtsave will result in faster runs but coarser plots and coarsely saved data, while a small value will result in slower runs but finer plots and larger data sets. Class: Scalar. Units: Time.

**Note:** The value of dtsave will not affect the accuracy of the actual integration.

- IMR(x):  $\Lambda_i$ . The inward migration rate for demographic group *i*. Class: xtype. Units: People/Time.
- mud(x):  $\mu_{id}$ . The natural death rate for demographic group *i*. Class: xtype. Units: Time<sup>-1</sup>.
- mum(x):  $\mu_{im}$ . The natural migration rate out of the population for demographic group *i*. Class: xtype. Units: Time<sup>-1</sup>.
- alpha(x):  $\alpha_i \in [0,1]$ . The susceptibility of a person in  $S_i$ . Class: xtype. Units: 1.

[Beta]: Note: [Beta] is not present in the input file.

The next 3 input parameters relate to this quantity.  $\beta_{kj} \in [0,1]$ . The infectivity of a person in  $I_{kj}$ . Class: xtautype. Units: 1.

beta(x):  $\beta_{kj}(k)$ . The relative infectivity of each demographic group. The sum of these parameters will be normalized to 1.

beta(tau):  $\beta_{kj}(j)$ . The relative infectivity of each infection stage. The sum of these parameters will be normalized to 1.

beta (Value of Integral): After normalized beta(x) and normalized beta(tau) have been raked, the resulting matrix will be multiplied by beta (Value of Integral). This parameter is equal to  $\sum_{k=1}^{n} \sum_{j=1}^{m} \beta_{kj}$ . Care must be taken when this parameter is chosen to ensure that  $\beta_{kj} \leq 1 \quad \forall \ k,j$ . The code will **not** return a warning if this condition is violated.

[Gamma]: Note: [Gamma] is not present in the input file.

The next 3 input parameters relate to this quantity.  $\gamma_{ij}$ . The rate of disease progression for a person in demographic group i and infection stage j. Class: xtautype. Units: Time<sup>-1</sup>.

gamma(x): The relative rates of disease progression for each demographic group. The sum of these parameters will be normalized to 1.

gamma(tau): The relative rates of disease progression for each infection stage. The sum of these parameters will be normalized to

gamma (Value of Integral): After normalized gamma(x) and normalized gamma(tau) have been raked, the resulting matrix will be multiplied by gamma (Value of Integral). This parameter is equal to  $\sum_{i=1}^{n} \sum_{j=1}^{m} \gamma_{ij}$ .

[DeltaI]: Note: [DeltaI] is not present in the input file.

The next 3 input parameters relate to this quantity.  $\delta_{ij}$ . The disease-induced death rate for demographic group i in infectious stage j. Class: xtautype. Units: Time<sup>-1</sup>.

deltaI(x):

This is the relative death rate for each demographic group. The sum of these parameters will be normalized to 1. If they are all 0, no normalization will take place.

deltaI(tau):

This is the relative death rate for each infection stage. The sum of these parameters will be normalized to 1. If they are all 0, no normalization will take place.

deltaI (Value of Integral):

After normalized deltaI(x) and normalized deltaI(tau) have been raked, the resulting matrix will be multiplied by deltaI (Value of Integral). This parameter is equal to  $\sum_{n=1}^{\infty} \sum_{k=1}^{\infty} f(x)$ 

 $\sum_{i=1}^{n} \sum_{j=1}^{m} \delta_{ij}.$ 

plotfigures: Gives different options for plotting the results. §3.6.1 has more details. Class: Scalar.

- 0: Prints no plots.
- Prints out separate plots for each demographic group. Each plot will show the susceptible population, the population in each infected stage, and the recovered population in that group.
- Prints out separate plots for each demographic group. Each plot will have the susceptible population, the total infected population in that demographic group (sums the infected population over the different infection stages) and the recovered population.
- Prints out separate plots for each demographic group. Each plot will have the relative fraction of the population of each infection stage out of the total infected population in that demographic group.
- Prints out one graph that has the total susceptible population, the total infected population and the total recovered population.

Flag to command MATLAB to kill plots before run is killimages: over. Class: Scalar.

- Leaves the plots on the screen. You will need to kill them manually.
- Hitting any key will kill the plots one by one. 1:

printdata:

Flag to print data to screen. If printdata is 0, no data will be printed to screen. If it is 1, the code will print to screen, the total population, the total infected population, the population in each subgroup and their time rate of change. In the display, where n is the number of demographic groups and m is the number of infection stages,  $y(1) \dots y(n)$  will correspond to  $S_1 \dots S_n$ ;  $y(n+1) \dots y(2n)$  will correspond to  $I_{11} \dots I_{n1}$ ;  $y(2n+1) \dots y(3n)$  will correspond to  $I_{12} \dots I_{n2}$ ; and so on, with  $y((m \times n) + 1) \dots y((m+1) \times n)$  corresponding to  $I_{1m} \dots I_{nm}$  and  $y(((m+1) \times n) + 1) \dots y((m+2) \times n)$ corresponding to  $R_1 \dots R_n$ . yt(i) will correspond to the time derivative of y(i). Class: Scalar.

PlotJac: Flag that tells the code to plot eigenvalues of the Jacobian (if the disease-free equilibrium exists). If PlotJac is set to 1, the code will plot the real part of the eigenvalues of the Jacobian of the equations for the infected group at the disease-free equilibrium. If it is set to 0, these plots will not be printed out. The Jacobian will be calculated, regardless. Class: Scalar.

#### **3.4.2** XTfile

This file contains the data for the x and  $\tau$  endpoints — which determine the number of demographic groups and infection stages. The file needs to be in ASCII format. The file is read using load. It should contain one column vector with the first entry specifying the number of x endpoints (ie. one greater than the number of demographic groups desired). If the first entry is n, the next n entries should be the x endpoints and there will be (n-1) demographic groups. The remaining entries are the  $\tau$  endpoints. All endpoints should be in strictly ascending order. If the first entry does not give the correct number of x endpoints, there will be an error which may or may not be reported by the code. For example, the XTfile containing,

would create 3 demographic groups divided in the intervals (0, 8], (8, 25] and (25, 100]; and 4 infection stages divided into the intervals (1, 2], (2, 3], (3, 4] and (4, 5].

This information is used to create xtype, tautype and xtautype classes for the parameters and the variables. The units of x can be of your choosing or x may be unitless. The units of  $\tau$  should be time.

#### **3.4.3** SIfile

This file is used to create an xtype class for the initial susceptible population; and an xtautype class for the initial infected population. (An xtype class is also created for the initial recovered population but the number of people there is automatically set to zero.) The units for these classes are people.

For FlagData set to 'FullMP', SIfile needs to be in ASCII format. The file is read using load. The first column is the number of people in the susceptible section of each demographic group. The second column is the number of people in the first infection stage in each demographic group. The third column is the number of people in the second infection stage in each demographic group and so on.

The first row corresponds to the people in the first demographic group, the second row to the people in the second demographic group and so on.

The number of rows must be the same as the number of demographic groups specified in XTfile, while the number of columns must be 1 more than the number of infection stages specified in XTfile (the first column contains the

susceptible group).

For example, for SIfile containing the following information,

```
100 0 5 0 0
500 0 0 3 2
300 1 8 0 0
```

the initial conditions would be

$$S_1 = 100$$
  $I_{11} = 0$   $I_{12} = 5$   $I_{13} = 0$   $I_{14} = 0$   $R_1 = 0$   $S_2 = 500$   $I_{21} = 0$   $I_{22} = 0$   $I_{23} = 3$   $I_{24} = 2$   $R_2 = 0$   $S_3 = 300$   $I_{31} = 1$   $I_{32} = 8$   $I_{33} = 0$   $I_{34} = 0$   $R_3 = 0$ 

with 3 demographic groups and 4 infection stages.

**Note:** The number of demographic groups and infection stages specified in SIfile must be consistent with the data in XTfile.

For FlagData set to 'FullEP', SIfile needs to be in the same format as the 'FullMP', but the input data is in endpoint format (so there will be 1 extra row and 1 extra column). The actual interpolated values will also depend on the endpoints specified in XTfile.

For FlagData set to 'SparseMP', SIfile needs to be in ASCII format. It is read using fscanf. The first n entries, where n is the number of demographic groups specified in XTfile, need to be the initial susceptible population in each demographic group. The next entries for the number of infected people in each infected subgroup should come in groups of 3. Out of each triplet, the first entry is the demographic group, the second entry is the infection stage and the third entry is the number of infected people. The number of infected people in all demographic groups and infection stages that are not specified by this file are set to 0.

For example, for SIfile containing,

the initial conditions would be

$$S_1 = 100$$
  $I_{11} = 0$   $I_{12} = 5$   $I_{13} = 0$   $I_{14} = 0$   $R_1 = 0$   $S_2 = 500$   $I_{21} = 0$   $I_{22} = 0$   $I_{23} = 3$   $I_{24} = 2$   $R_2 = 0$   $S_3 = 300$   $I_{31} = 1$   $I_{32} = 8$   $I_{33} = 0$   $I_{34} = 0$   $R_3 = 0$ 

with 3 demographic groups and 4 infection stages.

**Note:** The number of demographic groups and infection stages specified in SIfile must be consistent with the data in XTfile.

For FlagData set to 'SparseEP', the file needs to be in the same format as the 'SparseMP', but the input data is in endpoint format. There will need to be one more entry for the susceptible population. The entries for the infected population will also be for the endpoint values so the actual interpolated midpoint values will also depend on the endpoints specified in XTfile.

#### 3.4.4 MMfile

This file determines the parameters that describe the mixing between the different demographic groups (either  $q_{ik}$  or  $p_{ik}$  and  $c_i$ ). The format of this file is determined by MMflag.

If MMflag is set to 'QCData', then the code directly reads in the q and c data, calculates p and proceeds as described in §1.1.4. This file is read using the load command, and should be in ASCII format. It should contain n rows and (n+1) columns. The first column corresponds to c while the remaining n columns correspond to q. The file should be of the format:

**Note:** The number of demographic groups in this file must be equal to the number specified in XTfile.

If MMflag is set to 'MixingMatrix', the code reads in the total number of contacts between the different groups per unit time and then calculates c and p. This file is read using the load command and should be in ASCII format. The file should contain an  $n \times n$  symmetric matrix where n is the number of demographic groups (should be equal to the number defined in XTfile). This matrix should contain the total number of contacts (by all people) between the different demographic groups, per unit time. The units of M are (Number of Contacts)/Time. The unit of time here must be consistent with the unit of time used in sp.in for the other parameters that have time in their dimension.

This option allows for easy interfacing between this code and TRANSIMS<sup>6</sup>. Demographic data can be collected from TRANSIMS and stored in a file in the above format which can then be read by the code. However, care must be taken to ensure that the number of people used to create the mixing matrix must be the same as the total initial population. Otherwise, the average number of contacts per person that this code calculates will be inconsistent with the data in the mixing matrix.

An example of a valid MMfile for 3 demographic groups with MMflag = MixingMatrix is

```
67 45 12
45 377 128
12 128 35.
```

Here the people in demographic group 1 have a total of 67 contacts within their own group, 45 contacts with the people in demographic group 2 and 12 contacts with the people in demographic group 3, per unit time. The people

 $<sup>^6\</sup>mathrm{An}$  agent-based model of a virtual city that describes movement and interaction of people.

in demographic group 2 have a total of 45 contacts with group 1, 377 contacts amongst themselves and 128 contacts with group 3, per unit time. The people in group 3 have a total of 12 contacts with group 1, 128 contacts with people in group 2 and 35 amongst themselves, per unit time.

We describe the calculation of the parameters, p and c below.

Let  $M_{ik}$  be the total number of contacts between group i and group k per unit time, read from the input file. (This is the same quantity as  $T_{ik}$  in §1.1.4 but we use M here to denote an input read from a file.)

We define  $c_i$ , the preferred number of contacts per unit time of one person in group i, as the total number of contacts made by group i divided by the total initial population of group i in (14).

$$c_i = \frac{\sum_{k=1}^n M_{ik}}{N_i(0)}. (14)$$

We then define the preference for a contact between group i and group k using the definition for the total contacts (6) with the initial population data in (15).

$$p_{ik} = M_{ik} \frac{\sum_{l=1}^{n} c_l N_l(0)}{c_i N_i(0) \ c_k N_k(0)}.$$
 (15)

Note that now,  $p_{ik}$  is no longer restricted to being less than or equal to 1 and must be interpreted as a preference, not a probability. We do not solve for  $q_{ik}$ . These parameters no longer have the same interpretation as in [1], but this method serves as an efficient and consistent way of scaling the contacts between the demographic groups, while satisfying the balance constraints.

If MMflag is set to 'MixingMatrixPP', the code reads in the average number of contacts per person per unit time between the different groups and then calculates c and p. This file is read using the load command and should be in ASCII format. The file should contain an  $n \times n$  matrix (no longer needs to be symmetric) where n is the number of demographic groups (should be equal to the number defined in XTfile). This matrix should contain the average number of contacts **per person** between the different demographic groups, per unit time. The units of M are (Number of Contacts)/(Person·Time). The unit of time here must be consistent with the unit of time used in  $\operatorname{sp.in}$  for the other parameters that have time in their dimension.

**Note:** Although this matrix does not need to be symmetric, the matrix of the total number of contacts between the different demographic groups does need to be symmetric (because the total number of contacts between group i and group k must be equal to the total number of contacts between group k and group i). Thus, when each row of the matrix in MMfile is multiplied by the total population of that group, the resulting matrix must be symmetric.

An example of a valid MMfile for 3 demographic groups with population sizes  $N_1(0)=100,\,N_2(0)=50$  and  $N_3(0)=200$  for MMflag = 'MixingMatrixPP' is

7 5 2

10 7 8

1 2 5.

Here, each person in group 1 has, on average, 7 contacts with other people in group 1, 5 contacts with people in group 2 and 2 contacts with people in group 3. Similarly, each person in group 2 has, on average, 10 contacts with people in group 1, 7 contacts with other people in group 2 and 8 contacts with people in group 3. And each person in group 3 has, on average, 1 contacts with people in group 1, 2 contacts with people in group 2 and 5 contacts with other people in group 3. The total mixing matrix for this input file is

$$M = \left(\begin{array}{ccc} 700 & 500 & 200 \\ 500 & 350 & 400 \\ 200 & 400 & 1000 \end{array}\right).$$

The code calculates this total mixing matrix and then calculates c and p as it would if MMflag were set to 'MixingMatrix'.

**Note:** If the calculated total mixing matrix is not symmetric, the code will return an error and stop.

# 3.5 Algorithm

The ODE's are integrated using ode45. This method uses variable order Runge-Kutta (4 and 5) with a relative tolerance of  $10^{-6}$  and an absolute tolerance of  $10^{-11}$ . These may be varied, if desired, by changing the values of Eps and AbsEps, respectively, in dsdisp.m.

# 3.6 Output

The code has two forms of output:

- Some results and plots can be printed to the screen.
- Data is saved to files in the output directory.

#### 3.6.1 Displayed Results

There are numerous flags in sp.in that allow you to print various results to the screen. We will describe these in some detail below.

If printdata is set to 1, time, the populations of the different subgroups, their rate of change, the total population and the total infected population, at intervals of dtsave, will be displayed to the screen. On the screen,  $y(1) \dots y(n)$  correspond to  $S_1 \dots S_n$ ;  $y(n+1) \dots y(2n)$  correspond to  $I_{11} \dots I_{n1}$ ;  $y(2n+1) \dots y(3n)$  correspond to  $I_{12} \dots I_{n2}$ ; and so on, with  $y((m \times n) + 1) \dots y((m+1) \times n)$  corresponding to  $I_{1m} \dots I_{nm}$  and  $y(((m+1) \times n) + 1) \dots y((m+2) \times n)$  corresponding to  $R_1 \dots R_n$ . The terms y(i) correspond to the time derivative of y(i). Although this instant display of the results may be useful when setting up parameters, it will slow the code down.

Depending on the value of plotfigures, different plots may be displayed as shown in Table 3. There is currently no option to show the relative impact on disease spread of each infectious subgroup. We have yet to decide on the

final form of the expression for the relative impact, but we hope to add it to the model soon. The data is plotted from time equals 0 (after re-initialization — see §3.3 for more details) to the time specified in tfinal. The resolution of the plots is controlled by dtsave. The smaller dtsave is, the better the resolution. The plots are not saved by the code. If you do wish to save them, you will need to save them manually.

If killimages is set to 1, the code will wait for user-input to kill each figure. (Depending on the value of plotfigures there may be as many figures as demographic groups.) The figures will be killed sequentially from the first demographic group to the last. If you wish to view the plots while continuing to use MATLAB, set killimages to 0. You will then need to kill the figures manually.

- 0: Prints no plots.
- 1: Prints out separate plots for each demographic group. Each plot will show the susceptible population, the population in each infected stage, and the recovered population for that demographic group. Each plot has different line colors for the susceptible, infected and recovered population, but the same colour for the different infected subgroups; and the same linestyle for all curves. Also, there is no legend on these plots. The labels of the different subgroups are shown using the text command. The label is placed slightly above the maximum of that curve—so if there are a number of monotonically increasing curves, all their text labels will be placed on the right of the figure. This layout may not necessarily be visually pleasing. If you wish to show these data in a professional setting, I would recommend writing your own script to plot the data. You may copy and paste code from plotfig.m, if it helps.
- 2: Prints out separate plots for each demographic group. Each plot will have the susceptible population, the total infected population in that demographic group and the recovered population in that group. The infected population is summed over the different infection stages for each demographic group. These plots do have different linestyles and line colors. They have a legend and the lines are drawn 2pt thick.
- 3: Prints out separate plots for each demographic group. Each plot will have the relative fraction of the population of each infection stage out of the total infected population in that demographic group. Again, each plot has the same line colors and linestyles. There is no legend and the curves are labeled by text which appears slightly above the maximum value of that curve. It may again be necessary to write your own plotting routines to display these graphs in a more visually pleasing manner.
- 4: Prints out one graph that has the total susceptible population, the total infected population and the total recovered population of the whole system. This plot does have different linestyles and colors. There is a legend and the lines are drawn 2pt thick.

Table 3: The different options for plotting data for values of plotfigures

If plotJac is set to 1, the real part of the eigenvalues of the Jacobian at the disease-free equilibrium will be plotted on the screen. The x-axis is simply a labelling of the eigenvalues while the y-axis is the real part of the eigenvalues. The different eigenvalues are shown by crosses.

#### 3.6.2 Saved Results

There are currently three files saved by the code. They contain the population of each subgroup at different times, the time to re-initialization and the Jacobian of the linearized system around the disease-free equilibrium. The files saved are:

- ytData.dat
- Time\_Init.dat
- JacTE.dat

These are all saved in the output directory. If you wish to use different names for these files you can change the values of ytfile, tinitfile and jacfile, respectively, in dsdisp.m.

### 1. ytData.dat:

This file contains the values of time, the population of the subgroups and their rates of change, at intervals of dtsave, from time t=0 (after reinitialization) to tfinal. These are stored in ASCII format in ytData.dat using the subroutine saveyt.m. The first column of ytData.dat contains the values of time. Values in columns 2 through (n+1) contain data for groups  $S_1$  through  $S_n$ . The next n columns contain data for subgroups  $I_{11}$  through  $I_{n1}$ . The n columns after that contain data for  $I_{12}$  through  $I_{n2}$  and so on. The last n columns contain data for  $R_1$  through  $R_n$ . The first row corresponds to time 0. The second row to time dtsave, the third row to time  $2\times$ dtsave and so on.

You may use loadsirp.m to retrieve the data from ytData.dat. The subroutine loadsirp.m takes in 4 input parameters. The first parameter is the filename where the data is stored. The second parameter is a flag that determines the format of this file. This can be either 'ASCII' or 'MAT'. The third parameter is the number of demographic groups and the fourth parameter is the number of infection stages in the model. For retrieving data saved by dsdisp.m, use 'ytData.dat' for the first parameter, 'ASCII' for the second parameter and then enter the number of demographic groups and infection stages for the third and fourth parameters.

The function loadsirp.m has four output parameters. The first parameter, T is a column vector of time values from 0 to tfinal at intervals of dtsave. The second parameter, SP, is a matrix containing the information on the susceptible population. The first column corresponds to time t = 0: the second to time t = dtsave and so on — with each column

corresponding to a value of time defined in T. The first row contains the values of  $S_1$  at each of these times, the second row the values of  $S_2$  and so on, with the last row containing the values of  $S_n$ . The third output parameter, IP, contains the infected population values. This is a 3D array where each page corresponds to time defined in T. Each row corresponds to the demographic group and each column corresponds to the infection stage. The fourth output parameter, RP is the recovered population and has a similar structure to SP.

# Typing

### > help loadsirp

in MATLAB in the directory dsmodel/code will also produce this information on the format of the output.

#### 2. Time\_Init.dat:

This file contains the time at which the code re-initializes the population as described in §1.1.6. The file is saved in ASCII format and contains only a scalar.

### 3. JacTE.dat:

This file contains the Jacobian of the system (of only the infecteds) at the disease-free equilibrium. The Jacobian is calculated as described in  $\S 1.1.5$ . This file is also stored in ASCII format. It contains one matrix with all the terms of the Jacobian.

# 3.7 Sample Run

To run this code, open MATLAB and enter the directory, dsmodel/code. Then, type in

#### > dsdisp.

For sample runs, some input files have already been created. In the directory, <code>dsmodel/input</code> there are three subdirectories:

- AIDS4G
- AIDSDISP
- AIDSSP.

To run any of these models, copy all four input files from that subdirectory into dsmodel/input and from dsmodel/code in MATLAB run dsdisp. This will run the code with the parameters set up for that model.

To run the code with your own parameters, it may also help to start with sp.in from one of these models and change that as you wish to keep the format of that file.

#### 3.8 **User-Defined Equations**

To allow the user to expand this model to include more dynamics, such as behaviour change or migration between demographic groups, we have included functions that can be changed by the user to modify the system of equations.

The system variables, S, I and R are stored as one large column vector, y. The format of y is the same as that in §3.6.1. The first n terms,  $y(1) \dots y(n)$ , correspond to  $S_1 \dots S_n$ . The next n terms,  $y(n+1) \dots y(2n)$ , correspond to  $I_{11} \dots I_{n1}$ ;  $y(2n+1) \dots y(3n)$  correspond to  $I_{12} \dots I_{n2}$ ; and so on, with  $y((m \times$  $(n) + 1) \dots y((m+1) \times n)$  corresponding to  $I_{1m} \dots I_{nm}$  and  $y(((m+1) \times n) + 1) \dots y((m+1) \times n)$ 1) ...  $y((m+2) \times n)$  corresponding to  $R_1 ... R_n$ .

To change the derivatives, you may add or subtract terms in fuser.m. This subroutine returns a column vector (with the same format as y) that is added to the system of equations (1). Let us call the output vector of fuser.m, u. Adding a term to u(1) will add that term to  $S_1$ ; adding it to u(n) will add it to  $S_n$ ; u(n+1) to  $I_{11}$  and so on.

For example, to convert the model to an SIRS model (16), with a recovery rate,  $\rho$ , fuser.m would need to return the vector (17). However, the user would need to input the new parameter,  $\rho$ , directly in fuser.m

$$\frac{dS_i}{dt} = \Lambda_i - (\mu_{iS} + \lambda_i(t))S_i + \rho_i R_i$$
(16a)

$$\frac{dI_{i1}}{dt} = \lambda_i(t)S_i - (\gamma_{i1} + \mu_{i1})I_{i1}$$
(16b)

$$\frac{dS_i}{dt} = \Lambda_i - (\mu_{iS} + \lambda_i(t))S_i + \rho_i R_i \qquad (16a)$$

$$\frac{dI_{i1}}{dt} = \lambda_i(t)S_i - (\gamma_{i1} + \mu_{i1})I_{i1} \qquad (16b)$$

$$\frac{dI_{ij}}{dt} = \gamma_{i,j-1}I_{i,j-1} - (\gamma_{ij} + \mu_{ij})I_{ij} \quad \text{for } 2 \le j \le m \qquad (16c)$$

$$\frac{dR_i}{dt} = \gamma_{im}I_{im} - (\rho_i + \mu_{iR})R_i \qquad (16d)$$

$$\frac{dR_i}{dt} = \gamma_{im}I_{im} - (\rho_i + \mu_{iR})R_i \tag{16d}$$

for  $1 \le i \le n$ .

$$u = \begin{pmatrix} \rho_{1}R_{1} \\ \rho_{2}R_{2} \\ \vdots \\ \rho_{n}R_{n} \\ 0 \\ \vdots \\ 0 \\ \vdots \\ 0 \\ -\rho_{1}R_{1} \\ -\rho_{2}R_{2} \\ \vdots \\ -\rho_{n}R_{n} \end{pmatrix}$$

$$(17)$$

Also, any changes to fuser.m, will require corresponding changes to jacuserTE.m to keep the equations consistent. The output of jacuserTE.m is a matrix, following the format of  $\S 1.1.5$ . This output is added to the jacobian calculated in getjacobianTE.m. In the above example, as no changes are made to the equations for I, the jacobian is unchanged.

# 3.9 Killing Execution

To kill execution at any time, type in Ctrl + c. As some data is saved into output files at the end of the run, in most cases, not all the data will be saved. Some variables in MATLAB's working memory may be changed.

# 4 Bugs and Modifications

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